# Vitamin D and Lipid Profiles in Infertile PCOS and Non-PCOS Females

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## ABSTRACT

**Objective:** This research is aimed to explore the relationship between vitamin D and lipid profile in females with PCOS and non-PCOS infertile female subjects.

**Study Design:** Comparative descriptive study.

**Place and Duration of the Study:** Department of Biological and Biomedical Sciences, The Aga Khan University, Karachi, Pakistan and Jinnah Postgraduate Medical Centre, Karachi, Pakistan in collaboration with the Australian Concept Infertility Medical Centre, from February 2021 to March 2023.

**Methodology:** A total of 180 infertile women with 120 PCOS and 60 non-PCOS were enrolled. The lipid profile and BMI of the patients were acquired from desk records, and vitamin D was estimated by enzyme-linked immunosorbent assay (ELISA). Participants were classified according to their vitamin D levels as sufficient (30-100 ng/ml), insufficient (20-29 ng/ml), or deficient (below 20 ng/ml). Median, interquartile range, frequency, and percentages were described. Statistical significance was calculated by Mann-Whitney U and Chi-square tests with p-values of 0.05.

**Results:** Females with PCOS had significantly low vitamin D ($p < 0.001$). Total cholesterol, low-density lipoprotein, very low-density lipoprotein, and triglyceride levels were significantly increased, and high-density lipoprotein cholesterol (HDL) was less in comparison to the non-PCOS group ($p < 0.001$). A significant increase in total cholesterol, triglycerides, low-density lipoproteins, and very low-density lipoproteins was found in the vitamin D deficient subgroup compared with insufficient or sufficient groups ($p = 0.05$).

**Conclusion:** The study provides a link between females with PCOS and abnormalities in lipid profile. Decreased vitamin D levels in females with PCOS were linked with an abnormal lipid profile characterised by rise in cholesterol, triglycerides, and low-density lipoproteins which may lead to metabolic abnormalities.

**Key Words:** *Vitamin D, Polycystic ovary syndrome, Metabolic syndrome, Body mass index, Lipid profile.*

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a syndrome that mainly disturbs women during reproductive years, having a prevalence rate between 9% and 18%.[1] PCOS may lead to insulin resistance (IR), obesity, dyslipidaemia, diabetes mellitus (DM), hypertension, cardiovascular disease (CVD), and cancer.[2,3] Women having PCOS are more likely to develop dyslipidaemia than women without PCOS.[4] Dyslipidaemia in PCOS is characterised by decreased high-density lipoprotein cholesterol (HDL) levels and elevated triglyceride (TGs) and low-density lipoprotein cholesterol (LDL) levels.[4]

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Vitamin D plays a crucial role in the growth of the skeleton through calcium and phosphorus metabolism and many other functions.[5] However, vitamin D can take part in other diseases, like DM and CVD.[6,7] Nowadays, variation in vitamin D and their relation with metabolic factors in PCOS and without PCOS women remain debatable.[8] Some studies demonstrated that PCOS women had lower serum vitamin D as compared to women without PCOS, and vitamin D deficiency was interrelated with hyperinsulinemia, dyslipidaemia, and metabolic issues in PCOS patients.[8,9] However, other investigators have obtained diverse results that no diversity is seen between PCOS and non-PCOS.[10] Therefore, this research aimed to explore the association of vitamin D with the lipid profile of PCOS and non-PCOS infertile female subjects.

## METHODOLOGY

A descriptive comparative study was planned between February 2021 to March 2023 by the Department of Biological and Biomedical Sciences at The Aga Khan University and Jinnah Postgraduate Medical Centre in collaboration with The Australian Concept Infertility Medical Centre. A total of 180

subjects, 120 women with PCOS (cases) and 60 women without PCOS (control) were enrolled through convenient sampling. Infertile women with PCOS were included as 'cases' based on Rotterdam criteria: Occurrence of two from three standards, i.e., oligo and / or anovulation, extra androgenic action and / or appearance of polycystic ovaries on ultrasonography.[11] The cases were of all ethnicities, aged 18 to 45 years, infertile for more than two years. Healthy women of the same age with no evidence of polycystic ovary on ultrasound and a regular menstrual cycle were counted as comparison group (non-PCOS).

Infertility due to sperm defects in men, secondary fertility cases, as well as women with gynaecological tumours, diabetes mellitus, hypertension, hyperprolactinemia, thyroid conditions, adrenal disorders, currently on hormonal, oral contraceptives, antiepileptic drugs, or gonadotropins were omitted from the study. The Ethical Review Board of The Aga Khan University granted permission to conduct this study (ERC number 2021-4812-16633). After obtaining the informed written agreement, standard anthropometrical parameters, together with height, weight, waist circumference (WC), and hip perimeter were acquired from all of the patients. Clinical information on the lipid profile of all study participants was extracted from their records. The privacy of both, their medical and non-medical information was maintained. In addition to stratification into PCOS (120) and non-PCOS (60) females, participants were subcategorised according to their vitamin D levels into sufficient (30-100 ng/ml), insufficient (20-29 ng/ml), and deficient (<20 ng/ml).[12] Each participant provided 10ml of venous blood on the 2nd day of the menstrual cycle. In case of an irregular menstrual cycle, a sample was collected at any point of the cycle. The blood was centrifugated at 3000rpm for 20 minutes to obtain serum. Subsequently, the serum samples were frozen and reserved at -80°C for vitamin D assessment. The analysis of serum vitamin D was conducted through an ELISA kit (Catalogue no: VD315B).

The data analysis was done *via* IBM SPSS Statistics v27. The Kolmogorov-Smirnov test was applied to confirm the normality of the data. For quantitative data, the median and interquartile range, and for qualitative results, frequency and percentages were reported. Quantitative variables were compared using the Kruskal-Wallis H test and the Mann-Whitney U test. The Chi-square test was applied to check associations between the qualitative parameters. A p-value below 0.05 was stated as statistically significant.

## RESULTS

The median age of females with and without PCOS was 33 years and 33.5 years, respectively. Body mass index (BMI) of PCOS patients was significantly higher than non-PCOS ($p < 0.001$). The median total cholesterol, TGs, LDL, and very low-density lipoprotein were significantly raised, and HDL was low in females with PCOS than that of non-PCOS ($p < 0.001$, Table I).

Stratification of vitamin D levels of the study population revealed 80%, 60%, and 34% females with vitamin D deficiency, insufficiency, and sufficiency, respectively.

The distribution of PCOS and non-PCOS among different vitamin D levels showed that the highest proportion of females with PCOS, 69 individuals (57.5%), suffered from vitamin D deficiency.

Table II describes study variables in vitamin D stratified; deficient, insufficient, and sufficient subgroups. The median total cholesterol, TGs, LDL, and very low-density lipoprotein were significantly raised with low HDL in the vitamin D deficient subgroup as compared to insufficient and sufficient infertile females (p-value <0.001).

**Table I: Comparative analysis of the demographical characteristics and lipid profiles across the study groups.**

| Study Groups | Median (IQR) | | p-value |
|---|---|---|---|
| | Non-PCOS (n = 60) | PCOS (n = 120) | |
| Age (years) | 33.50 (6.75) | 33.00 (10.00) | 0.636 |
| Body mass index (kg/m$^2$) | 26.53 (6.36) | 28.93 (8.02) | <0.001* |
| **Lipid profile** | | | |
| Total cholesterol (mg/dL) | 178.00 (21.50) | 220.50 (21.00) | <0.001* |
| Triglycerides (mg/dL) | 134.00 (20.25) | 211.50 (69.00) | <0.001* |
| High-density lipoprotein (mg/dL) | 48.00 (7.75) | 32.00 (4.75) | <0.001* |
| Low-density lipoprotein (mg/dL) | 117.00 (14.75) | 137.00 (12.00) | <0.001* |
| Very low-density lipoprotein (mg/dL) | 23.50 (4.75) | 45.00 (14.75) | <0.001* |

*IQR: Inter-quartile range. Mann-Whitney U test was used. *Significant at 0.05 levels.*

## DISCUSSION

According to this study's findings, PCOS is associated with high cholesterol, LDL, and TGs, and lower HDL than non-PCOS. These findings are consistent with a meta-analysis which observed that women with PCOS had greater non-HDL and LDL cholesterol levels than those without PCOS.[13] This suggests that dyslipidaemia disturbs PCOS more commonly than non-PCOS.[14] Increased androgen levels were linked to phenotypic changes in lipid profiles as demonstrated by other studies, which show that androgens play a significant role in deranged lipid profile.[14,15]

This study shows a significantly increased BMI in PCOS than in non-PCOS women. One research also highlighted the relationship between PCOS and BMI and the higher incidence of obesity among PCOS-positive participants.[16] It revealed that PCOS is related to cardiac issues, with higher blood pressure and adverse lipid profiles in women with PCOS, regardless of their BMI.[17] The link between BMI and PCOS is further supported by studies in Brazil, which found higher BMI and waist circumference in PCOS patients along with worse cardio metabolic profiles.[18] Anothor research also found no statistically important relation among vitamin D levels and metabolic variables, waist-to-hip ratio (WHR), or BMI in women affected by PCOS.[19]

Vitamin D deficiency is a common issue affecting more than one billion people both adults and children worldwide.[8] PCOS women show a comparatively higher incidence of vitamin D deficiency than non-PCOS women, and vitamin D deficiency is related to ovulatory dysfunction, IR, and hyperandrogenism.[20,21] Hence, currently, several researches have been conducted to explore the vitamin D status of women with PCOS.[22,23]

**Table II: Evaluation of the demographical attributes and lipid profiles in relation to vitamin D levels.**

| Study Groups | Vitamin D levels - Median (IQR) | | | p-value |
|---|---|---|---|---|
| | Deficient (n = 80) | Insufficient (n = 66) | Sufficient (n = 34) | |
| Age (in years) | 33.00 (9.00) | 32.50 (6.25) | 33.50 (10.25) | 0.685 |
| Body mass index (kg/m$^2$) | 28.26 (7.20) | 28.00 (8.64) | 26.83 (5.16) | 0.262 |
| **Lipid profile** | | | | |
| Total cholesterol (mg/dL) | 218.00 (35.00) | 199.00 (49.00) | 190.00 (40.00) | 0.004* |
| High-density lipoprotein (mg/dL) | 34.00 (5.75) | 39.00 (15.25) | 39.00 (16.25) | 0.002* |
| Low-density lipoprotein (mg/dL) | 135.00 (15.50) | 126.50 (21.75) | 129.00 (26.25) | 0.013* |
| Very-low-density lipoprotein (mg/dL) | 43.00 (18.25) | 31.50 (22.75) | 25.50 (23.25) | 0.015* |
| Triglycerides (mg/dL) | 200.50 (89.00) | 147.50 (76.00) | 152.00 (81.25) | 0.011* |

*IQR: Inter-quartile range. Kruskal-Wallis H test was applied. *Significant at 0.05 levels.*

Facts from this study's findings observed that vitamin D was relatively low, and the prevalence of deficient and insufficient vitamin D was meaningfully raised in PCOS women than in non-PCOS women, these results were comparable to the earlier study.[8] The frequency of vitamin D deficiency in PCOS women ranges from 67% to 85%.[1] Another study by Bindayel *et al.* found that mean vitamin D levels were meaningfully reduced in Saudi PCOS women than in non-PCOS women.[12] In this study, the authors demonstrated a significant association between vitamin D levels, dyslipidaemia, and obesity in individuals with PCOS. This study recommends that the BMI, vitamin D, and lipid profiles of all infertile females with PCOS should be estimated and corrected to ensure successful results in infertility treatments. The study had a limited sample size based on which generalisability of results could not be possible.

## CONCLUSION

Reduced vitamin D levels in females with PCOS are related to metabolic abnormalities which can be manifested by an increase in the cholesterol, TGs, and LDL. This study provides a link between females with PCOS and abnormalities in lipid profile. Future researches should explicitly address the mechanisms intricating in the interplay of vitamin D levels, obesity, and lipid profile in females with PCOS.

### ETHICAL APPROVAL:

Ethical approval was acquired from the Ethical Review Committee of The Aga Khan University Hospital, Karachi, Pakistan (ERC number 2021-4812-16633).

### PATIENTS' CONSENT:

Informed consent was obtained from the patients.

### COMPETING INTEREST:

The authors declared no conflict of interest.

### AUTHORS' CONTRIBUTION:

AA: Designed the study, conducted the analysis, drafted the manuscript, and revised it for important intellectual content.
SMA: Drafted the work and revised it critically for important intellectual content.
RR: Conceived, designed, and supervised the manuscript.
All authors approved the final version of the manuscript to be published.

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